

PATENT COOPERATION TREATY



PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

| | |
|---|---|
| Date of mailing (day/month/year) 10 February 1998 (10.02.98) | |
| International application No. PCT/NL97/00354 | Applicant's or agent's file reference PCT 0591 |
| International filing date (day/month/year) 24 June 1997 (24.06.97) | Priority date (day/month/year) 25 June 1996 (25.06.96) |
| Applicant BEEKMAN, Nico, Johannes, Christiaan, Maria et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
22 January 1998 (22.01.98)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

A. Addae-Ruesch

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | | |
|--|---|--|---|
| Applicant's or agent's file reference PCT 0591 | FOR FURTHER ACTION | | see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |
| International application No. PCT/NL 97/ 00354 | International filing date (day/month/year) 24/06/1997 | (Earliest) Priority Date (day/month/year) 25/06/1996 | |
| Applicant STICHTING INSTITUUT VOOR DIERHOUDERIJ ... et al. | | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☒ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

VACCINE COMPRISING ANTIGENS BOUND TO CARRIERS THROUGH LABILE BONDS

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. _____ ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL 97/00354

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K39/385 A61K39/00 A61K39/23 //C07K14/015,C07K7/23

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | WO 92 12995 A (MEDOR LAB FUER BIOCHEMIE UND K) 6 August 1992 see page 2, line 8 - page 7, line 21 see page 10, line 30 - line 36 --- | 1-5,15, 22,26,27 |
| X | EP 0 491 077 A (GA INVESTMENT S A) 24 June 1992 see page 4, line 4 - line 8 see claims 1,13 --- | 1-5,15, 22,26,27 |
| X | WO 95 08348 A (HENRY M JACKSON FOUNDATION FOR) 30 March 1995 see page 27 - page 28; figure 2 --- | 1-5,15, 22,26,27 |
| -/-- | | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

*** Special categories of cited documents :**

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

20 October 1997

Date of mailing of the international search report

10. 11. 97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Fernandez y Branas, F

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 97/00354

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------------|
| X | US 5 256 641 A (YATVIN MILTON B ET AL) 26 October 1993 see column 3, line 55 - column 4, line 60 see column 5, line 56 - column 6, line 19 see column 8, line 6 - line 49 --- | 1-5,15, 22,26,27 |
| X | WO 93 02706 A (COMMW SCIENT IND RES ORG) 18 February 1993 see page 11, line 10 - line 27; claims 1,7,8 --- | 1-4,8,9, 15,22, 26,27 |
| X | WO 94 25060 A (LADD ANNA E ;WANG CHANG YI (US); ZAMB TIMOTHY (US)) 10 November 1994 see example 15 --- | 1-4, 22-27 |
| X | EP 0 431 327 A (HOECHST AG) 12 June 1991 see the whole document | 1-4,22, 26,27 |
| Y | | 9-11, 23-25 |
| Y | WO 90 11298 A (STICHTING CENTR DIERGENEESKUND) 4 October 1990 see the whole document --- | 9,23-25 |
| Y | WO 94 17098 A (INMUNOLOGIA Y GENETICA APLICAD ;CASAL ALVAREZ JOSE IGNACIO (ES); V) 4 August 1994 see the whole document --- | 10,23-25 |
| Y | RICHARDSON J. ET AL: "Neutralization sensitivity and accesibility of continuous B cell epitopes of the feline immunodeficiency virus envelope" THE JOURNAL OF GENERAL VIROLOGY, vol. 77, April 1996, pages 759-777, XP002041747 see page 761, figure 1 and left column, first and second paragraphs ----- | 11,23-25 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/NL 97/00354

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| WO 9212995 A | 06-08-92 | DE 4101394 A | 23-07-92 |
| EP 0491077 A | 24-06-92 | AU 657935 B | 30-03-95 |
| | | AU 9081791 A | 22-07-92 |
| | | CA 2098021 A | 20-06-92 |
| | | CZ 9301186 A | 16-02-94 |
| | | WO 9211368 A | 09-07-92 |
| | | EP 0563093 A | 06-10-93 |
| | | HU 66437 A | 28-11-94 |
| | | JP 6507303 T | 25-08-94 |
| | | SK 63693 A | 06-10-93 |
| WO 9508348 A | 30-03-95 | AU 678613 B | 05-06-97 |
| | | AU 7839194 A | 10-04-95 |
| | | CA 2171942 A | 30-03-95 |
| | | EP 0720485 A | 10-07-96 |
| | | JP 9502978 T | 25-03-97 |
| | | US 5651971 A | 29-07-97 |
| US 5256641 A | 26-10-93 | US 5149794 A | 22-09-92 |
| | | AU 4670093 A | 31-01-94 |
| | | EP 0650371 A | 03-05-95 |
| | | JP 7509227 T | 12-10-95 |
| | | WO 9401138 A | 20-01-94 |
| | | US 5543389 A | 06-08-96 |
| | | US 5543390 A | 06-08-96 |
| | | US 5543391 A | 06-08-96 |
| WO 9302706 A | 18-02-93 | AU 657565 B | 16-03-95 |
| | | CA 2114125 A | 18-02-93 |
| | | EP 0596959 A | 18-05-94 |
| WO 9425060 A | 10-11-94 | AU 6670294 A | 21-11-94 |
| | | CA 2161445 A | 10-11-94 |
| | | EP 0708656 A | 01-05-96 |
| | | FI 955101 A | 21-12-95 |
| | | JP 9503742 T | 15-04-97 |
| | | NO 954279 A | 27-12-95 |
| EP 0431327 A | 12-06-91 | DE 3937412 A | 16-05-91 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/NL 97/00354

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|--|--|
| EP 0431327 A | | AT 137118 T DE 59010300 D ES 2087111 T JP 4054131 A | 15-05-96 30-05-96 16-07-96 21-02-92 |
| WO 9011298 A | 04-10-90 | NL 8900726 A CA 2049325 A DE 69007616 D DE 69007616 T EP 0464124 A ES 2050435 T JP 4504256 T US 5484592 A | 16-10-90 24-09-90 28-04-94 30-06-94 08-01-92 16-05-94 30-07-92 16-01-96 |
| WO 9417098 A | 04-08-94 | ES 2065254 A ES 2089966 A AU 680264 B AU 7004894 A CA 2132742 A EP 0647655 A NZ 259882 A | 01-02-95 01-10-96 24-07-97 15-08-94 24-07-94 12-04-95 24-03-97 |

09/24,009

PATENT COOPERATION TREATY

REN

From the INTERNATIONAL SEARCHING AUTHORITY

10-1-98

Sum PCT

To:
 VEREENIGDE OCTROOIBUREAU
 Attn. SMULDERS, Th.A.H.J
 Nieuwe Parklaan 97
 2587 BN Den Haag
 NETHERLANDS

*prel en 25-1-98
 nat. reg. fase
 25-2-98*

NOTIFICATION OF TRANSMITTAL OF
 THE INTERNATIONAL SEARCH REPORT
 OR THE DECLARATION

bericht gezonden
 aan
 ad.

MAP

(PCT Rule 44.1)

Date of mailing
 (day/month/year) 10/11/1997

Applicant's or agent's file reference
 PCT 0591

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
 PCT/NL 97/00354

International filing date
 (day/month/year) 24/06/1997

Applicant
 STICHTING INSTITUUT VOOR DIERHOUDERIJ ... et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicants's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.


4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 bis.1 and 90 bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Maria Van der Hoeven

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SMULDERS, Th., A., H., J.
Vereenigde Octrooibureaux
Nieuwe Parklaan 97
NL-2587 BN The Hague
PAYS-BASDate of mailing (day/month/year)
09 March 1998 (09.03.98)Applicant's or agent's file reference
PCT 0591International application No.
PCT/NL97/00354

IMPORTANT NOTIFICATION

International filing date (day/month/year)
24 June 1997 (24.06.97)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

STICHTING INSTITUUT VOOR
DIERHOUDERIJ EN DIERGEZONDHEID
(ID-DLO)
Edelhertweg 15
NL-8219 PH Lelystad
Netherlands

State of Nationality

NL

State of Residence

NL

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

STICHTING INSTITUUT VOOR
DIERHOUDERIJ EN DIERGEZONDHEID
Edelhertweg 15
NL-8219 PH Lelystad
Netherlands

State of Nationality

NL

State of Residence

NL

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority ☐ other:The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Nicola Wolff

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

09/214009

565

Copy for the Elected Office (EO/US)

PCT/NL97/00354

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SMULDERS, Th., A., H., J.
Vereenigde Octrooibureaux
Nieuwe Parklaan 97
NL-2587 BN The Hague
PAYS-BAS

| | |
|---|---|
| Date of mailing (day/month/year) 21 December 1998 (21.12.98) | IMPORTANT NOTIFICATION |
| Applicant's or agent's file reference PCT 0591 | |
| International application No. PCT/NL97/00354 | International filing date (day/month/year) 24 June 1997 (24.06.97) |

1. The following indications appeared on record concerning:
- ☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

DANISH VETERINARY INSTITUTE FOR
ANIMAL VIRUS RESEARCH
Lindholm
DK-4771 Kalvehave
Denmark

State of Nationality

DK

State of Residence

DK

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:
- ☐ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

STICHTING INSTITUUT VOOR DIERHOUDERIJ EN
DIERGEZONDHEID
Edelhertweg 15
NL-8219 PH Lelystad
The Netherlands

State of Nationality

NL

State of Residence

NL

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:
The applicant indicated in Box 1 assigned the rights to the applicant indicated in Box 2.

4. A copy of this notification has been sent to:

- ☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Mougamadou Abidine

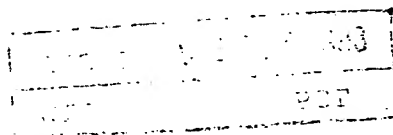
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



| | | |
|---|---|---|
| Applicant's or agent's file reference PCT 0591 | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/NL 97/ 00354 | International filing date (day/month/year) 24/06/1997 | Priority date (day/month/year) 25/06/1996 |
| International Patent Classification (IPC) or national classification and IPC A61K39/385 | | |
| Applicant STICHTING INSTITUUT VOOR DIERHOUDERIJ ... et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


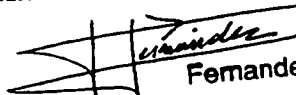
2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of 3 sheets.

3. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| | |
|---|---|
| Date of submission of the demand 22/01/1998 | Date of completion of this report 1. 10. 98 |
| Name and mailing address of the IPEA/  European Patent Office, P.B. 5818 Patendaan 2 NL-2280 HV Rijswijk - Netherlands Tel.: (+ 31-70) 340-2040, Tx. 31 651 epo nl Fax: (+ 31-70) 340-3016 | Authorized officer  Fernandez y Branas, F.J. 01949 Telephone No. |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NL97/00354

I. Basis of the report

1. This report has been drawn up on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*

☐ the international application as originally filed

☒ the description, pages 1 - 27

pages

pages

, as originally filed

, filed with the demand

, filed with the letter of

☒ the claims, Nos.

Nos.

Nos.

Nos.

1 - 23

, as originally filed

, as amended under Article 19

, filed with the demand

, filed with the letter of

26- 06- 98

☒ the drawings, sheets / fig. 1

sheets / fig.

sheets / fig.

, as originally filed

, filed with the demand

, filed with the letter of

2. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.

☐ the drawings, sheets / fig.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2 (c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NL97/00354

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|--------------------------|--------|--------|-----|
| Novelty | Claims | 1 - 23 | YES |
| | Claims | | NO |
| Inventive Step | Claims | 1 - 23 | YES |
| | Claims | | NO |
| Industrial Applicability | Claims | 1 - 23 | YES |
| | Claims | | NO |

2. Citations and Explanations

D1....EP- A- 431327 (HOECHST AKTIENGESELLSCHAFT)

D2....WO- A- 9508348 (HM JACKSON FOUNDATION)

D3....US- A- 5256641 (YATVIN MILTON B.)

1) In view of the prior art the subject matter of claims 1- 23 appears to be new in the sense of Article 33(2) PCT.

2) For the analysis of the inventive step of claims 1- 23 D1 is considered to be the closest prior art. D1 discloses vaccines comprising an antigenic peptide or protein linked to palmitic acid derivatives, e.g. Pam3Cys- Ser- Ser. The peptides are bound to the palmitoyl carrier through amide bonds, see D1, page 4 and claims. The difference between the present application and D1 is that in the present application palmitic acid is bound through a thioester or a disulphide bond to the synthetic peptide. In view of this difference the problem to be solved by the present application can be defined as the provision of alternative vaccines comprising fatty acid carriers.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NL97/00354

2.1.- Although thioester and disulphide bonds have been suggested in the prior art to link carriers and antigens (see for example D2 or D3), no indication or suggestion can be found in the prior art that would have induced the skilled person to produce vaccines by linking peptides to palmitic acid through thioester or disulphide bonds and bearing also in mind the results provided in the present application, see for example tables 2 and 5. Therefore the subject matter of claims 1- 23 involves an inventive step in the sense of Article 33(3) PCT.

CLAIMS

- 1 A vaccine comprising an antigen and a carrier compound which are directly or indirectly linked by a chemical bond that is labile and dissociates under certain physiological conditions.
- 5 2 A vaccine according to claim 1 in which said antigen dissociates from said carrier compound after the vaccine or preparation has been administered.
- 3 A vaccine according to claim 1 or 2 in which said antigen is a protein, a polypeptide, a synthetic peptide,
10 a carbohydrate, or a hapten.
- 4 A vaccine according to any of claims 1-3 in which said carrier compound is a protein or a fatty acid or a fatty acid peptide.
- 5 A vaccine according to any of claims 1-4 in which
15 said chemical bond is a thioester or a disulphide bond.
- 6 A vaccine according to any one of claims 1-5 in which said antigen is linked by thioester acylation to a fatty acid.
- 7 A vaccine according to claim 6 in which the antigen
20 is a synthetic peptide.
- 8 A vaccine according to any one of claims 4-7 in which the fatty acid is palmitic acid.
- 9 A vaccine according to claim 7 or 8 in which the synthetic peptide essentially consists of the amino acid
25 sequence /EHWSYGLRPGQHWSYGLRPG.
- 10 A vaccine according to claim 7 or 8 in which the synthetic peptide essentially consists of the amino acid sequence SDGAVQPDGGQPAVRNERATG.
- 11 A vaccine according to claim 7 or 8 in which the
30 synthetic peptide essentially consists of the amino acid sequence RAISSWKQRNRWEWPRD.

12 A vaccine according to claim 5 in which the antigen is a peptide and the carrier compound is another copy of said peptide coupled to a fatty acid.

13 A vaccine according to claim 12 in which the carrier
5 compound is an N-palmitoylated peptide.

14 A vaccine according to claim 12 or 13 in which the peptide essentially consists of the amino acid sequence SDGAVQPDGGQPAVRNERATG.

15 A vaccine preparation according to any of claims 1-14
10 together with pharmaceutically acceptable compound or adjuvant.

16 A composition comprising a synthetic peptide linked with a thioester bond to a fatty acid.

17 A composition according to claim 16 wherein the fatty
15 acid is palmitic acid.

18 A composition according to claim 16 or 17 wherein the peptide is selected from the group consisting of /EHWSYGLRPGQHWSYGLRPG, SDGAVQPDGGQPAVRNERATG and RAISSWKQRNRWEWPRD.

19 A composition comprising a synthetic peptide linked with a disulfide bond to a carrier compound comprising a fatty acid linked to another copy of said synthetic peptide.

20 A composition according to claim 19 wherein the fatty
25 acid is palmitic acid.

21 A composition according to claim 19 or 20 wherein the peptide is selected from the group consisting of /EHWSYGLRPGQHWSYGLRPG, SDGAVQPDGGQPAVRNERATG and RAISSWKQRNRWEWPRD.

22 A method for producing an immunogenic preparation comprising linking a synthetic peptide with a carrier compound via a chemical bond that is labile and dissociates under physiological conditions.

23 A method according to claim 22 wherein the carrier
35 compound is a fatty acid or a fatty acid coupled to another copy of said synthetic peptide.

PATENT COOPERATION TREATY

ONTVANGEN

06 OKT 1998

AMERSFOORT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

| | | |
|---------------------------|------------------------------|--------------------------------|
| To: | kopie 25/12.98 <i>Qu</i> | |
| SMULDERS, H. A. H. J. | IPEA/NL | |
| VEREENIGDE OCTROOIBUREAUX | 97 0 2 OKT. 1998 | |
| Nieuwe Parklaan | 2587 BN Den Haag | |
| PAYS-BAS | Beantwoord voort. def. | Bericht gezonden aan dd. |
| MAP <i>PCT 0591</i> | | |

NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year)

- 1. 10. 98

Applicant's or agent's file reference

PCT 0591

IMPORTANT NOTIFICATION

International application No.

PCT/NL 97/ 00354

International filing date (day/month/year)

24/06/1997

Priority date (day/month/year)

25/06/1996

Applicant

STICHTING INSTITUUT VOOR DIERHOUDERIJ ... et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Netherlands
Tel.: (+31-70) 340-2040, Tx. 31 651 epo nl
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Telephone No.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | |
|---|---|--|
| Applicant's or agent's file reference PCT 0591 | <div style="display: flex; justify-content: space-between;"> <div>FOR FURTHER ACTION</div> <div>See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)</div> </div> | |
| International application No. PCT/NL 97/ 00354 | International filing date (<i>day/month/year</i>) 24/06/1997 | Priority date (<i>day/month/year</i>) 25/06/1996 |
| International Patent Classification (IPC) or national classification and IPC A61K39/385 | | |
| Applicant STICHTING INSTITUUT VOOR DIERHOUDERIJ ... et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This **REPORT** consists of a total of 4 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
 These annexes consists of a total of 3 sheets.

3. This report contains indications and corresponding pages relating to the following items:
 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

| | |
|--|---|
| Date of submission of the demand 22/01/1998 | Date of completion of this report 1. 10. 98 |
| Name and mailing address of the IPEA/ European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Netherlands Tel.: (+ 31-70) 340-2040, Tx. 31 651 epo nl Fax: (+ 31-70) 340-3016 | Authorized officer Fernandez y Branas, F.J. Telephone No. 01949 |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NL97/00354

I. Basis of the report

1. This report has been drawn up on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*

☐ the international application as originally filed

☒ the description, pages 1 - 27
pages
pages

, as originally filed
, filed with the demand
, filed with the letter of

☒ the claims, Nos.

Nos.

Nos.

Nos.

1 - 23

, as originally filed
, as amended under Article 19
, filed with the demand
, filed with the letter of

26-06-98

☒ the drawings, sheets / fig. 1
sheets / fig.
sheets / fig.

, as originally filed
, filed with the demand
, filed with the letter of

2. The amendments have resulted in the cancellation of:

- ☐ the description pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets / fig.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2 (c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NL97/00354

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|--------------------------|--------|-------|-----|
| Novelty | Claims | 1- 23 | YES |
| | Claims | | NO |
| Inventive Step | Claims | 1- 23 | YES |
| | Claims | | NO |
| Industrial Applicability | Claims | 1- 23 | YES |
| | Claims | | NO |

2. Citations and Explanations

D1....EP- A- 431327 (HOECHST AKTIENGESELLSCHAFT)
D2....WO- A- 9508348 (HM JACKSON FOUNDATION)
D3....US- A- 5256641 (YATVIN MILTON B.)

1) In view of the prior art the subject matter of claims 1- 23 appears to be new in the sense of Article 33(2) PCT.

2) For the analysis of the inventive step of claims 1- 23 D1 is considered to be the closest prior art. D1 discloses vaccines comprising an antigenic peptide or protein linked to palmitic acid derivatives, e.g. Pam3Cys- Ser- Ser. The peptides are bound to the palmitoyl carrier through amide bonds, see D1, page 4 and claims. The difference between the present application and D1 is that in the present application palmitic acid is bound through a thioester or a disulphide bond to the synthetic peptide. In view of this difference the problem to be solved by the present application can be defined as the provision of alternative vaccines comprising fatty acid carriers.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/NL97/00354

2.1.- Although thioester and disulphide bonds have been suggested in the prior art to link carriers and antigens (see for example D2 or D3), no indication or suggestion can be found in the prior art that would have induced the skilled person to produce vaccines by linking peptides to palmitic acid through thioester or disulphide bonds and bearing also in mind the results provided in the present application, see for example tables 2 and 5. Therefore the subject matter of claims 1- 23 involves an inventive step in the sense of Article 33(3) PCT.

14. 07. 1998

Claims

1. A vaccine comprising an antigen and a fatty acid or fatty acid peptide carrier compound which are directly or indirectly linked by a thioester or a disulphide bond that is labile and dissociates under certain physiological conditions.

2 A vaccine according to claim 1 in which said antigen dissociates from said carrier compound after the vaccine or preparation has been administered.

3 A vaccine according to claim 1 or 2 in which said antigen is a protein, a polypeptide, a synthetic peptide, a carbohydrate, or a hapten.

4 A vaccine according to claim 3 in which the antigen is a synthetic peptide.

5 A vaccine according to any one of claims 1 - 4 in which the fatty acid is palmitic acid.

6 A vaccine according to claim 4 or 5 in which the synthetic peptide essentially consists of the amino acid sequence /EHWSYGLRPGQHWSYGLRPG.

7 A vaccine according to claim 4 or 5 in which the synthetic peptide essentially consists of the amino acid sequence SDGAVQPDGGQPAVRNERATG.

8 A vaccine according to claim 4 or 5 in which the synthetic peptide essentially consists of the amino acid sequence RAISSWKQRNRWEWPRD.

9 A vaccine according to any one of claims 1-4 in which the antigen is a peptide and the carrier compound is another copy of said peptide coupled to a fatty acid.

10 A vaccine according to claim 9 in which the carrier compound is an N-palmitoylated peptide.

11 A vaccine according to claim 9 or 10 in which the peptide essentially consists of the amino acid sequence SDGAVQPDGGQPAVRNERATG.

12 A vaccine preparation according to any of claims 1-11 together with pharmacautically acceptable compound or adjuvant.

13 A composition comprising a synthetic peptide linked with a thioester bond to a fatty acid.

14 A composition according to claim 13 wherein the fatty acid is palmitic acid.

15 A composition according to claim 13 or 14 wherein the peptide is selected from the group consisting of

/EHWSYGLRPGQHWSYGLRPG, SDGAVQPDGGQPAVRNERATG and RAISSWKQRNRWEWPRD.

16 A composition comprising a synthetic peptide linked with a disulfide bond to a carrier compound comprising a fatty acid linked to another copy of said synthetic peptide.

17 A composition according to claim 16 wherein the fatty acid is palmitic acid.

18 A composition according to claim 16 or 17 wherein the peptide is selected from the group consisting of

/EHWSYGLRPGQHWSYGLRPG, SDGAVQPDGGQPAVRNERATG and RAISSWKQRNRWEWPRD.

19 A method for producing an immunogenic preparation comprising linking a synthetic peptide with a fatty acid or fatty acid peptide carrier compound via a thioester or disalphide bond that is labile and dissociates under physiological conditions.

20 A method according to claim 19 wherein the fatty acid is palmitic acid.

21 A method according to claim 19 or 20 wherein the peptide is selected from the group consisting of

/EHWSYGLRPGQHWSYGLRPG SDGAVQPDGGQPAVRNERATG and RAISSWKQRNRWEWPRD.

22 An immunogenic preparation obtainable by a method according to any of claims 19-21..

23 A vaccine comprising an immunogenic preparation according to claim 22 together with pharmaceutically acceptable compound or adjuvant.